fascinATEing complexes

Justine deGruyter

Baran Lab Group Meeting
06.24.2017

Helpful resources.

[GM] Literature seminar, T. Mashiko (2007)
[review] *Top Organomet. Chem.* **2014**, *47*, 129.
[review] *Angew. Chem. Int. Ed.* **2007**, *46*, 3802.
[review] *Organometallics* **2006**, *25*, 1060.

Ate complexes *are salts formed from the stoichiometric reaction of a Lewis base and Lewis acid, wherein the acidic moeity formally increases its valence and becomes anionic.*

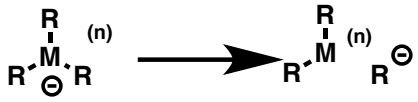
(Very) brief history.

- first alkali-metal ate complex, $NaZnEt_3$, synthesized in Wanklyn (1858)
- the term "ate" coined by Wittig (1951); first synthesis of magnesiate

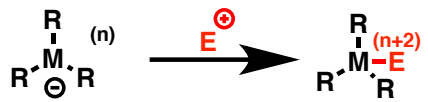
Structure and reactivity.

Two standard reaction pathways:

Non-oxidative charge neutralization (ligand transfer)



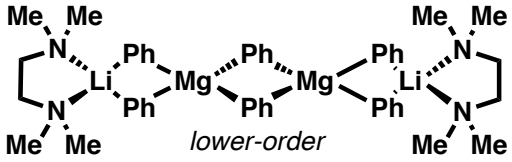
Oxidative charge neutralization (non-ligand transfer)



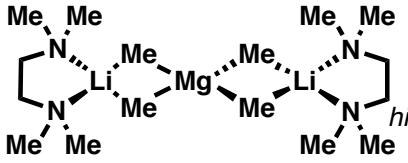
"Much of this synthetic and structural chemistry has a synergic element to it, in the sense that compounds with a heterobimetallic (ate) combination of an alkali metal (usually Li, Na, or K) and magnesium or zinc or aluminum, can effect (often surprising) reactions which cannot be replicated by the corresponding homometallic (non-ate) alkali-metal, magnesium, zinc, or alumnium compounds." (Mulvey, 2007)

- enhanced solubility in organic solvents is a reliable indicator of ate formation
- two types: contact-ion pair (CIP) and solvent-separated ion pair (SSIP)
- lower-order: $(AM)MR_3$, higher-order: $(AM)_2MR_4$

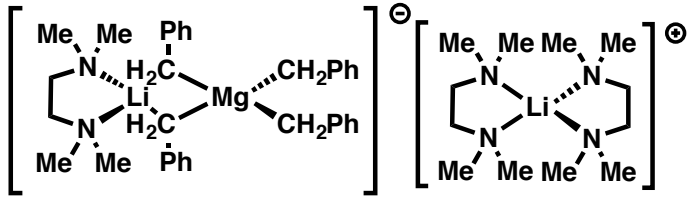
Weiss motifs.



lower-order



higher-order

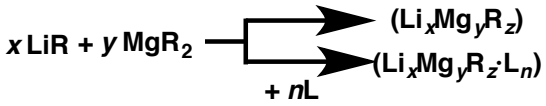


solvent-separated higher order

Magnesium ate ("Magnesiates" or "Magnesates").

alkyllithium > lithium trialkylmagnesate > alkylmagnesium

"Ordinary" structure.



Molecular architecture construction is a two-stage process:
- *anchoring* bonds: stronger, more covalent (α-based Mg–R interactions)
- *ancillary* bonds: more ionic, enable lithium ions to affix to framework (CIPs)

Two common formulations: R_3ZnLi and R_4ZnLi_2.

"Extraordinary" structure.

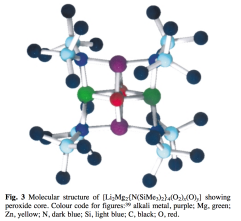
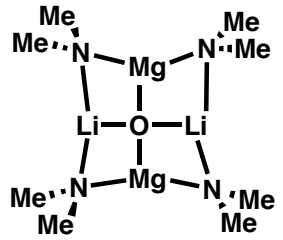


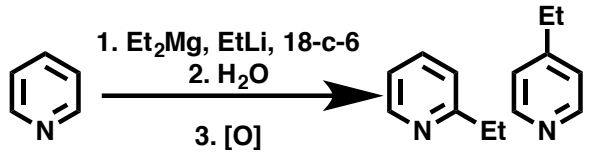
Fig. 3 Molecular structure of $[Li_2Mg_2\{N(SiMe_3)_2\}_2(O_2)_2(O)_2]$ showing peroxide core. Colour code for figures:[39] alkali metal, purple; Mg, green; Zn, yellow; N, dark blue; Si, light blue; C, black; O, red.

≡



"... a special type of chemistry beyond the scope of mainstream organometallic reagents is operating here."

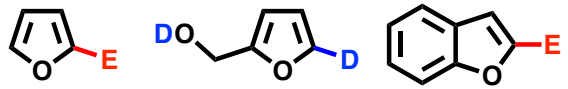
Reactions of diethylmagnesium–ethyllithium solutions with pyridine.
Richey. *Tet. Lett.* **1985**, *26*, 275.



minor *major*

Et_2Mg or EtLi alone lead exclusively to 1,2-add'n

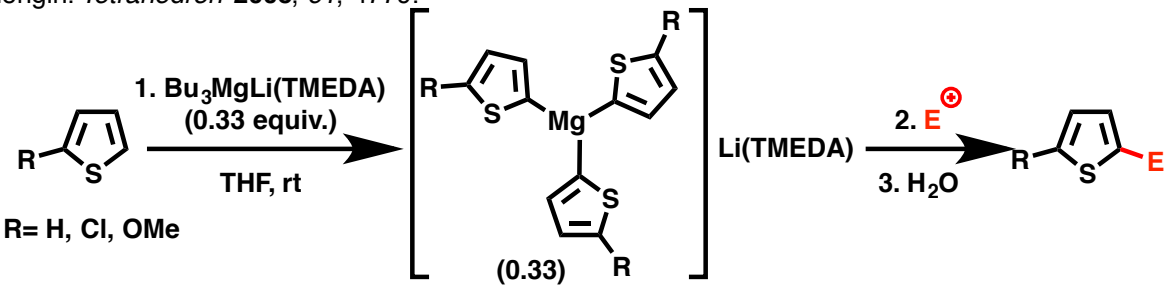
Deprotonation of furans using lithium magnesates. Mongin. *Tet. Lett.* **2005**, *46*, 7989.



(65–85%) *D_2O quench (48%)* *(85–89%)*

*can be trapped with E or engaged in a Pd-cat. cross-coupling event with 2-bromopyridine

Deprotonation of thiophenes using lithium magnesates.
Mongin. *Tetrahedron* **2005**, *61*, 4779.



R= H, Cl, OMe
(0.33)
Li(TMEDA)

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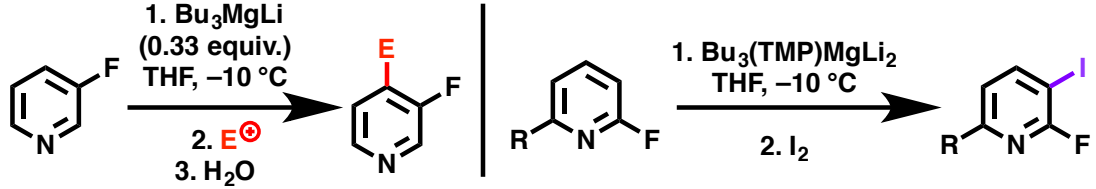
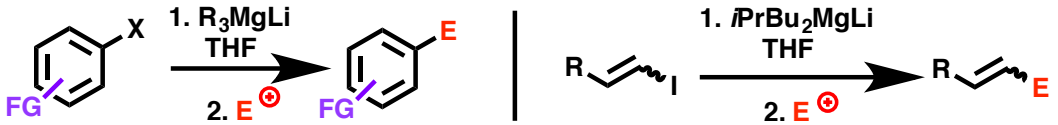
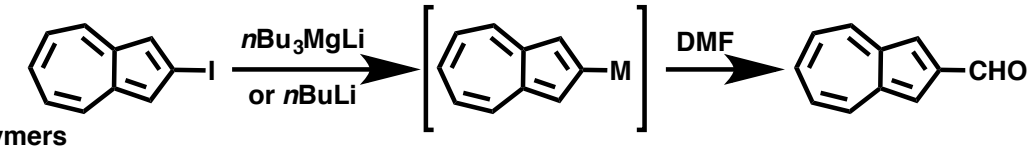
Deprotonation of fluoro aromatics using lithium magnesates.
Mongin. *Tet. Lett.* **2004**, *45*, 6697.



Halogen–magnesium exchange via trialkylmagnesates for the preparation of aryl and alkenyl-magnesium reagents. Oshima. *Angew. Chem. Int. Ed.* **2000**, *39*, 2481.



Preparation of azulenyllithium and magnesium reagents utilizing halogen–metal exchange reaction of several iodoazulenes with organolithium or magnesium ate complex.
Ito. *Tet. Lett.* **2004**, *45*, 2891.

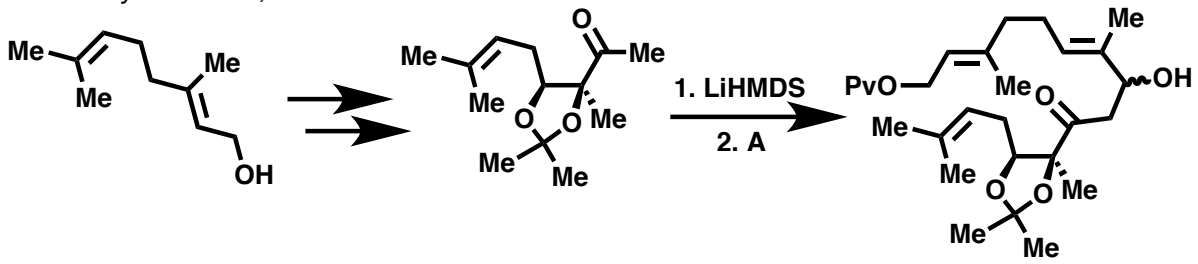


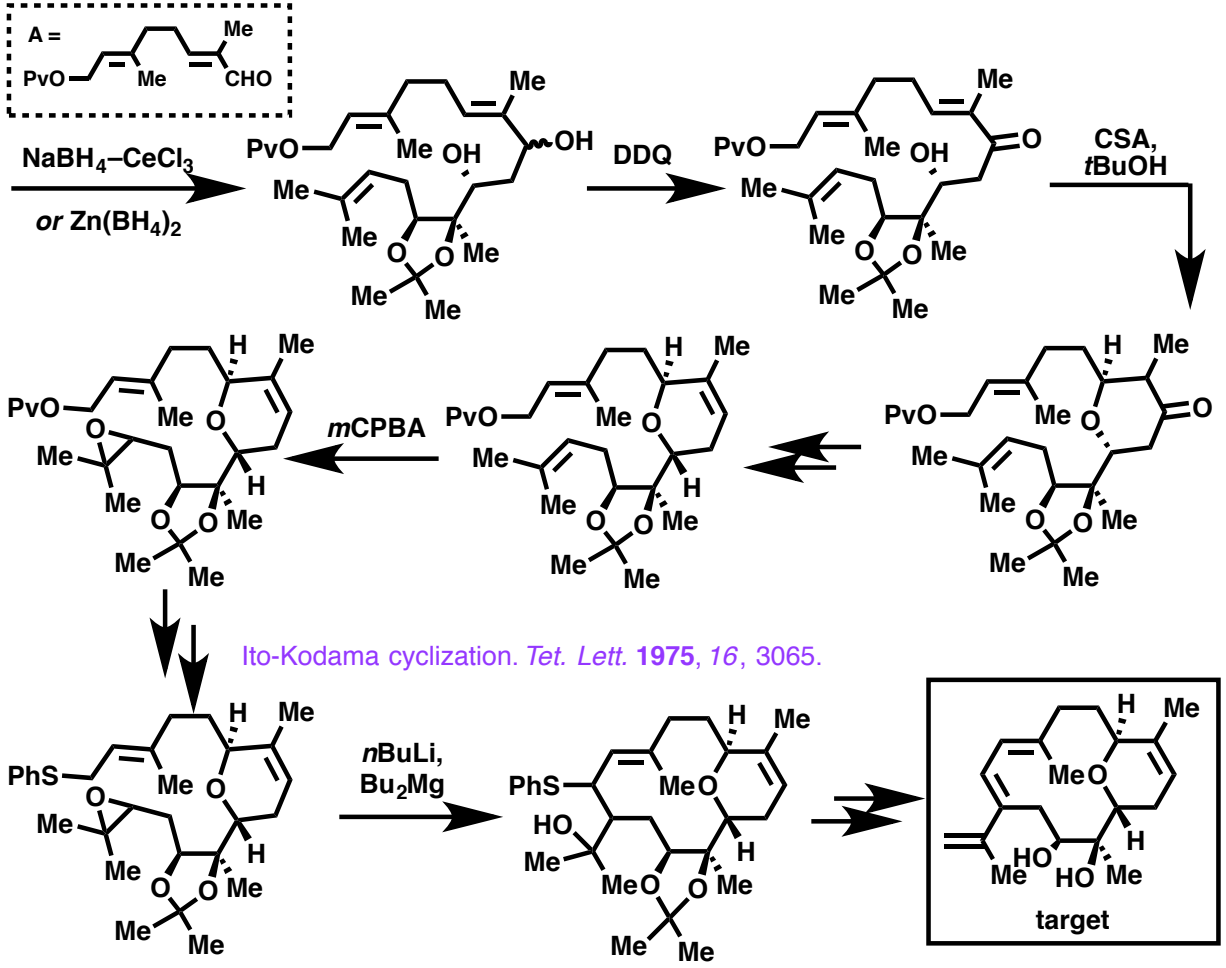
Polymers

Effects of dibutylmagnesium on alkyllithium-initiated polymerizations.
Hsieh. *Macromolecules.* **1986**, *19*, 299.

"Although...(*n*-Bu)(*s*-Bu)Mg (DCM) was not suitable as the sole initiator to polymerize butadiene and sytrene, its "ate" complex with... (*sec*-BuLi)... could initate the polymerization of both."
- Dispersity of 1.06 obtained in all cases; indicative of a "living" anionic polymerization.

Enantiospecific synthesis of the 14-membered diene unit of methyl sarcophytoate.
Nakata. *Synlett.* **1997**, 899.





Zincates.

[review] Recent developments in the synthetic and structural chemistry of lithium zincates.
Wheatley. *New. J. Chem.* **2004**, *28*, 435.

[review] s-Block metal inverse crowns: Synthetic and structural synergism in mixed alkali metal–magnesium (or zinc) amide chemistry.
Mulvey. *Chem. Commun.* **2001**, 1049.

[first reports] Wanklyn. *Liebigs Ann.* **1858**, *108*, 67.; Wanklyn. *Proc. R. Soc. London* **1858**, *9*, 341.

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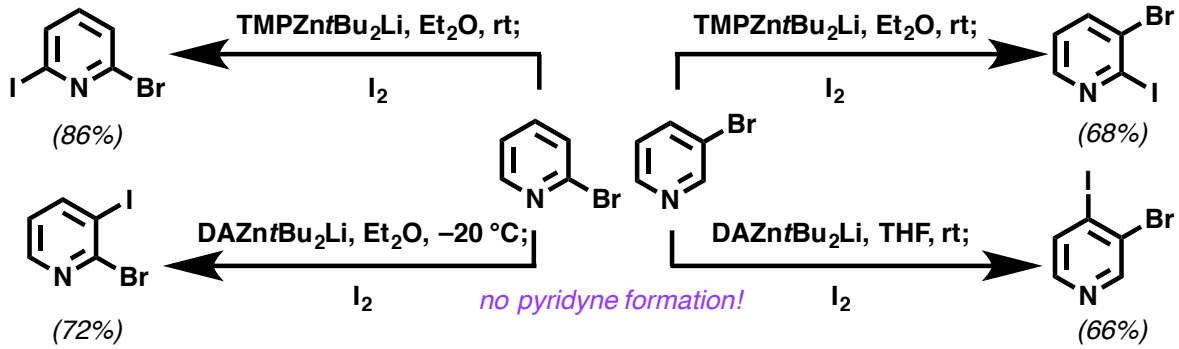
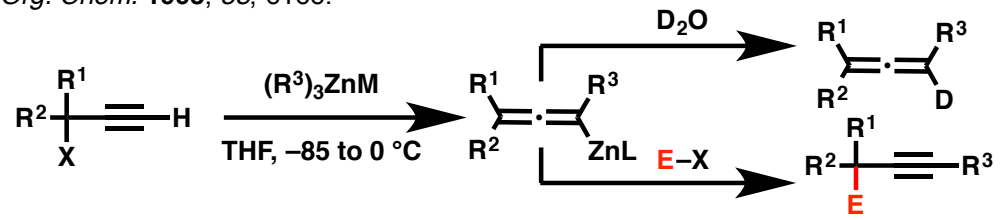
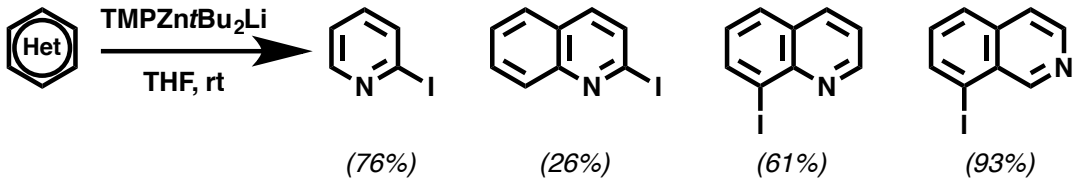
Regiocontrolled deprotonative-zincation of bromopyridines using aminozincates.
Kondo. *Chem. Commun.* **2001**, *2450.*



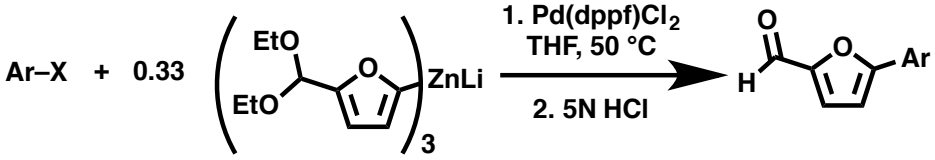
Reaction of propargylic substrates with triorganozincates: A novel method for the preparation of allenic zinc reagents associated with carbon–carbon bond formation.
Oku. *J. Org. Chem.* **1993**, *58*, 6166.



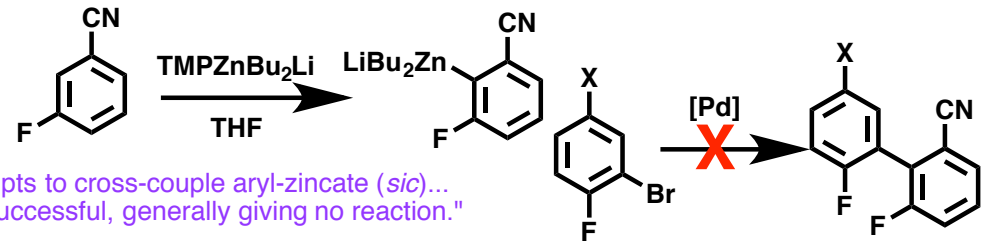
TMP–Zincate as highly chemoselective base for directed ortho metalation.
Kondo. *J. Am. Chem. Soc.* **1999**, *121*, 3539.



Synthesis of 5-pyridyl-2-furaldehydes via palladium-catalyzed cross-coupling with triorganozincates.
Gauthier. *Org. Lett.* **2002**, *4*, 375.



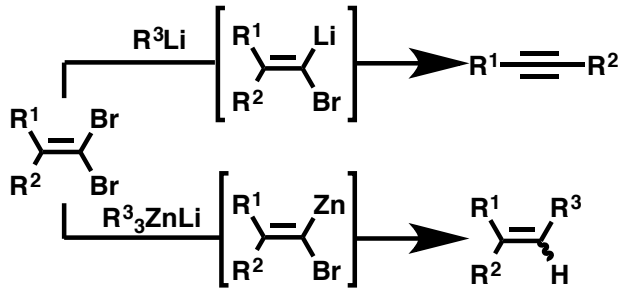
Palladium-catalyzed regioselective arylation of imidazo[1,2-*b*][1,2,4]triazine: Synthesis of an $\alpha_{2/3}$-selective GABA agonist.
Gauthier. *J. Org. Chem.* **2005**, *70*, 5938.



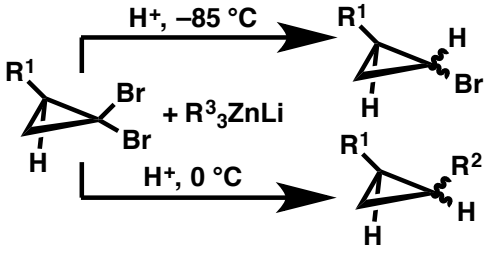
"All attempts to cross-couple aryl-zincate (*sic*)... were unsuccessful, generally giving no reaction."

"We believe the complete lack of reactivity... is due to the electron-withdrawing effects of the aryl substituents."

Generation and alkylation reaction of 1-bromoalkenyl-zincate. Oku. *Tet. Lett.* **1988**, *29*, 3821.



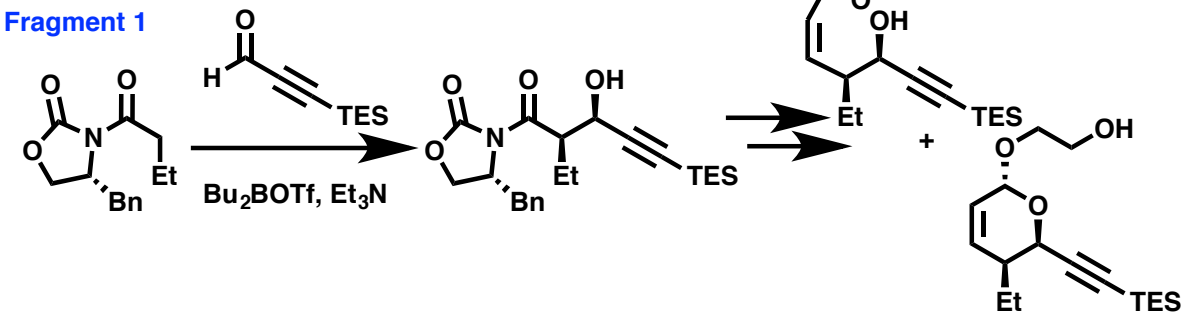
Generation and alkylation reaction of lithium 1-halocyclopropylzincate.
Oku. *Tet. Lett.* **1989**, *30*, 6035.



see also: *J. Org. Chem.* **1993**, *58*, 2958.; *Tetrahedron* **1994**, *50*, 7987.

A highly convergent total synthesis of leustroducsin B.
Trost. *J. Am. Chem. Soc.* **2015**, *137*, 11594.

Fragment 1



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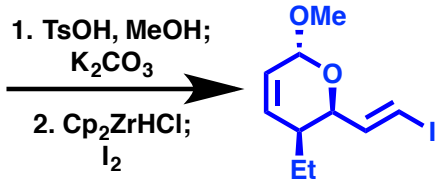
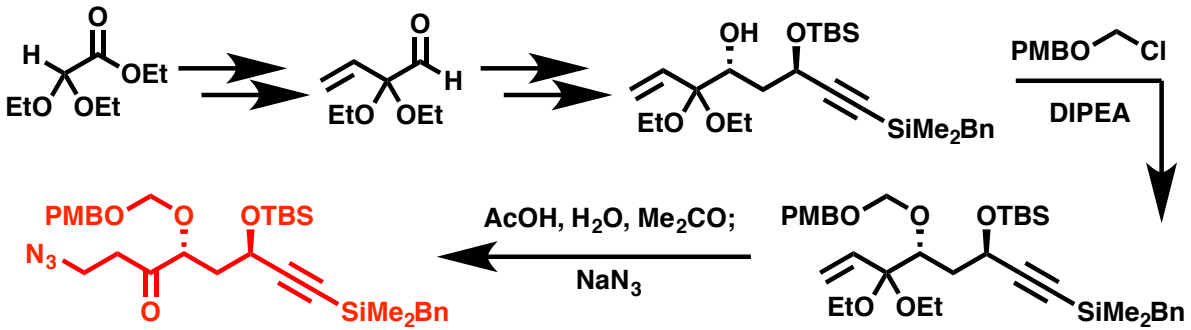


Fragment 2



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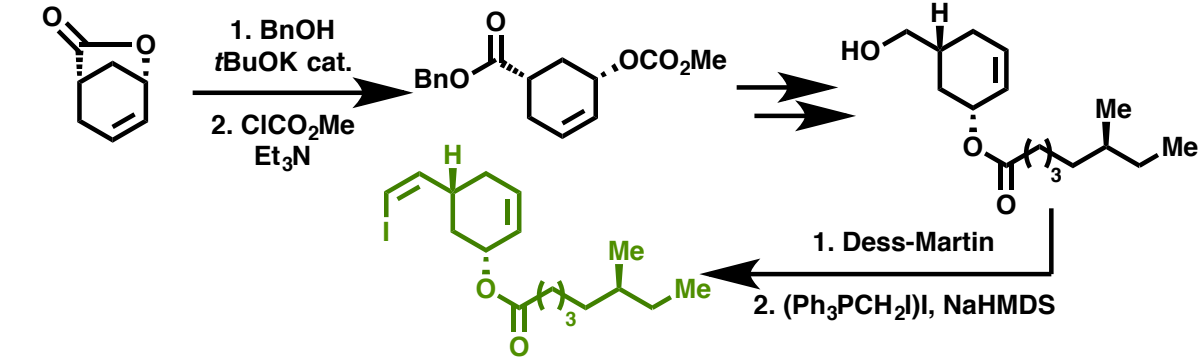
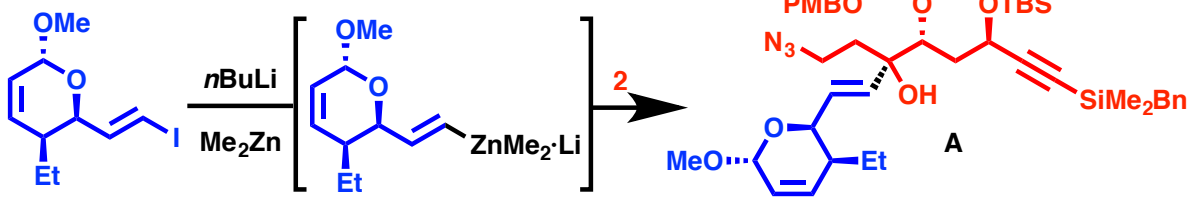
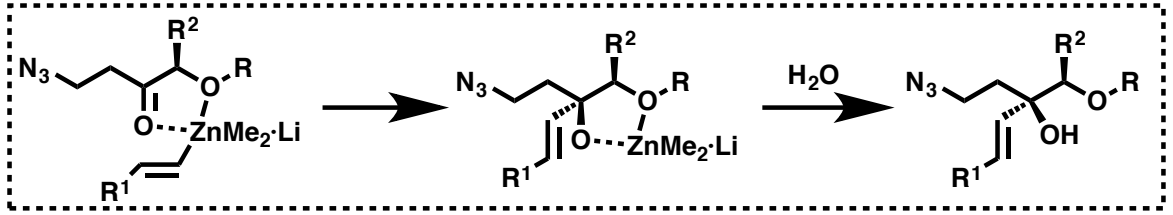
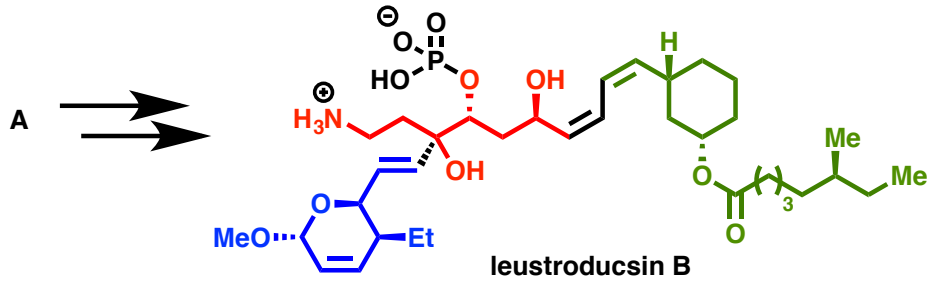


Chelation-controlled addition of 1 and 2

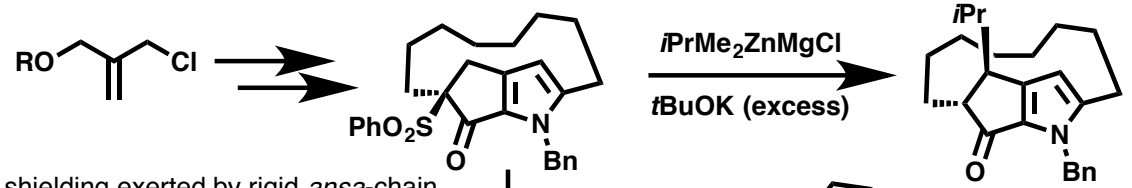




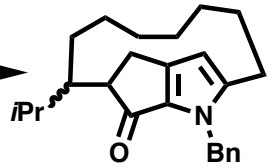


leustroducsin B

Total synthesis of roseophilin.
Fürstner. *J. Am. Chem. Soc.* **1998**, *120*, 2817.

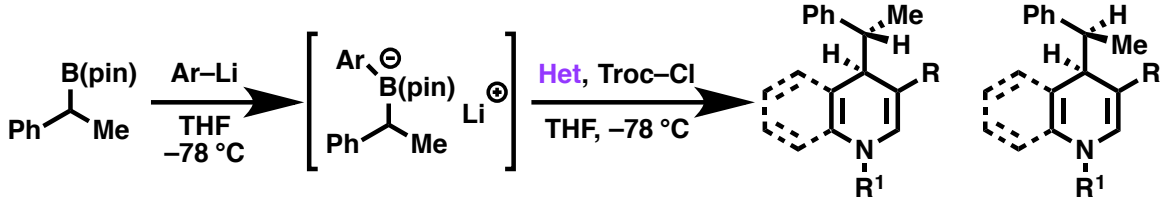


- shielding exerted by rigid *ansa*-chain provides facial guidance in Michael add'n
- forces protonation of enolate to occur from the same side
- corresponding cuprate proved ineffective



possible pathway to undesired

Boronates.
Asymmetric addition of chiral boron-ate complexes to cyclic iminium ions.
Aggarwal. *Chem. Sci.* **2014**, *5*, 602.



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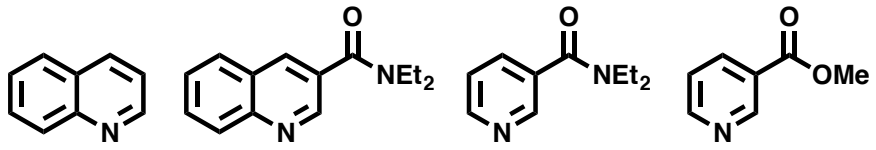
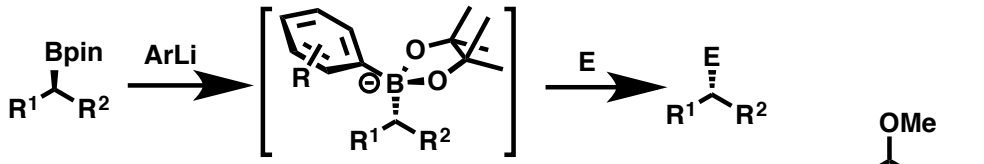
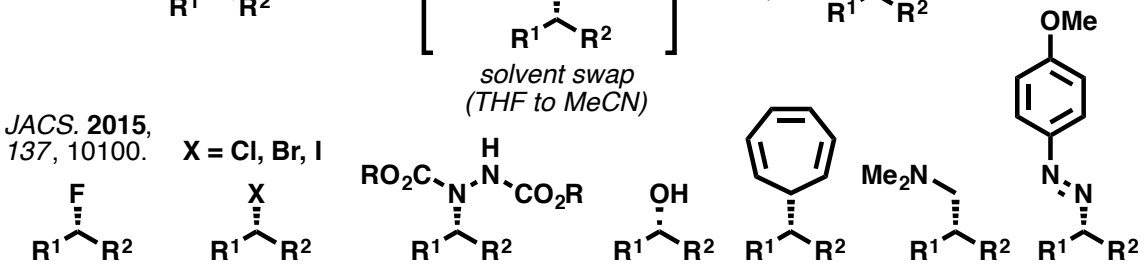


Ate complexes of secondary boronic esters as chiral organometallic-type nucleophiles for asymmetric synthesis. Aggarwal. *J. Am. Chem. Soc.* **2011**, *133*, 16794.

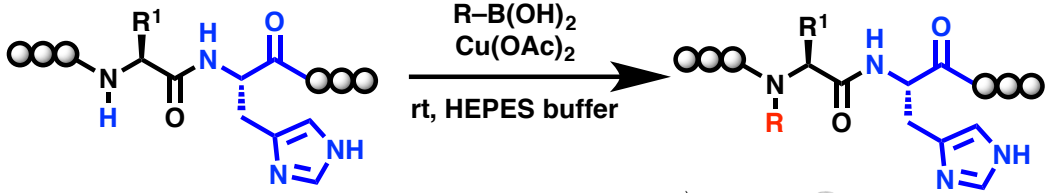
Synthesis of enantioenriched alkylfluorides by the fluorination of boronate complexes. Aggarwal. *J. Am. Chem. Soc.* **2015**, *137*, 10100.

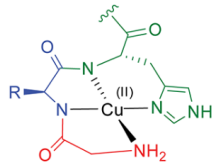


JACS. **2015**, *137*, 10100.

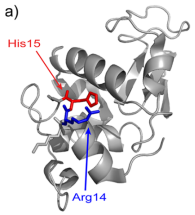


Histidine-directed arylation/alkenylation of backbone N–H bonds mediated by copper(II). Ball. *J. Am. Chem. Soc.* **2016**, *138*, 7472.



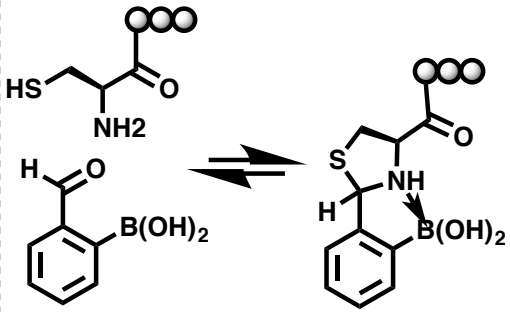


copper-bound ATCUN motif, illustrating activation of amide backbone N–H neighboring a His residue

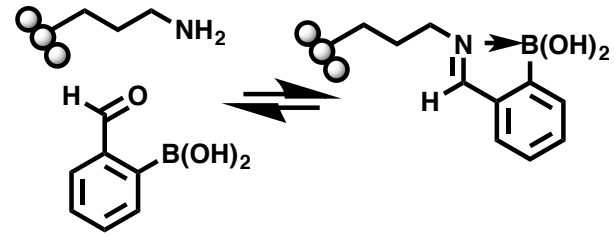


lysozyme with solitary His

Fast and selective labeling of N-terminal cysteines at neutral pH via thiazolidino boronate formation. Gao. *Chem. Sci.* **2016**, *7*, 4589.

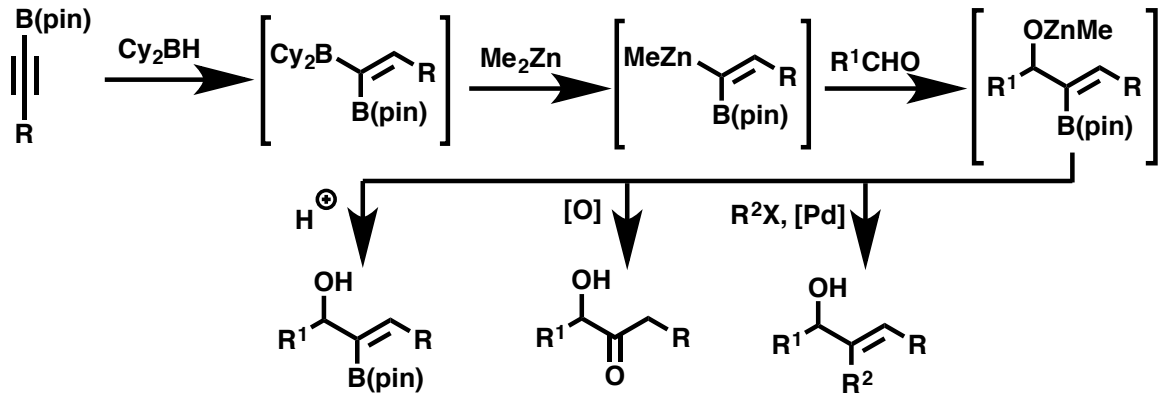


Iminoboronates: A new strategy for reversible protein modification.
Gois. *J. Am. Chem. Soc.* **2012**, *134*, 10299.

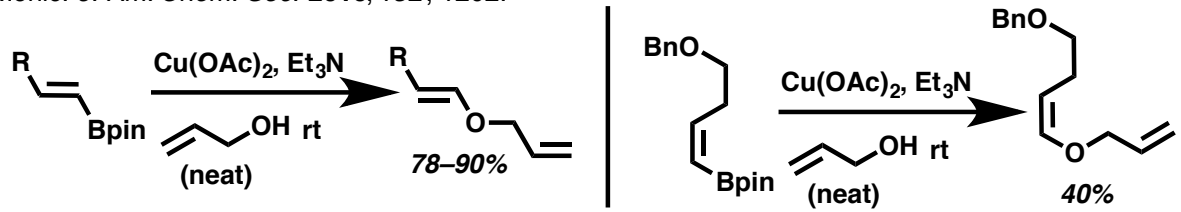


Applications of 1-alkenyl-1,1-heterobimetallics in the stereoselective synthesis of cyclopropylboronate esters, trisubstituted cyclopropanols and 2,3-disubstituted cyclobutanones.
Walsh. *J. Am. Chem. Soc.* **2009**, *131*, 6516.

improper use of nomenclature?



Copper-promoted coupling of vinyl boronates and alcohols: A mild synthesis of allyl vinyl ethers.
Merlic. *J. Am. Chem. Soc.* **2010**, *132*, 1202.



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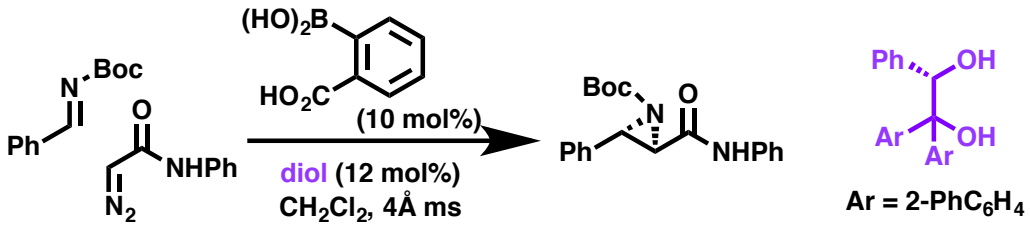
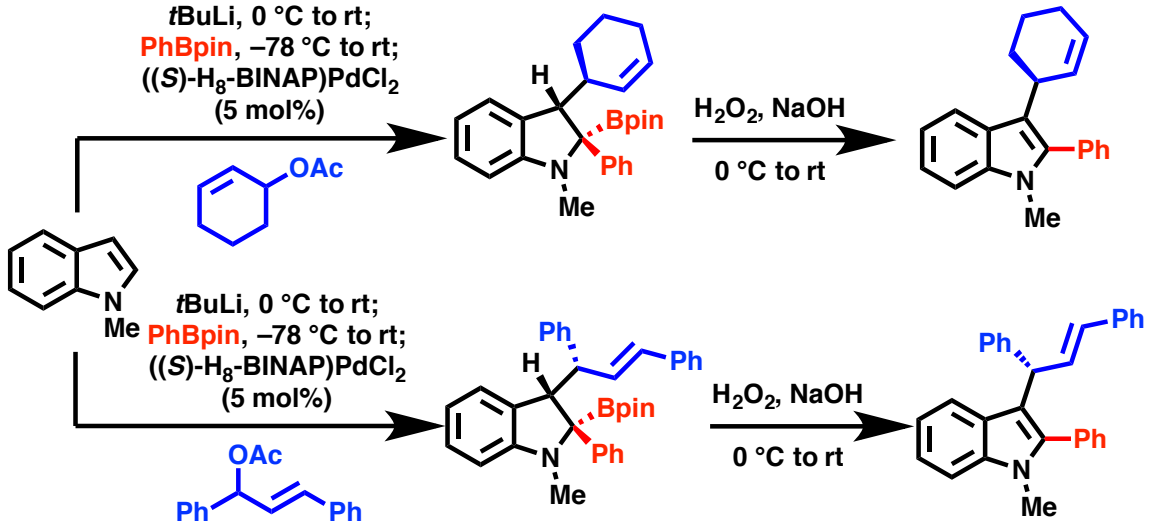
In situ assembled boronate ester assisted chiral carboxylic acid catalyzed asymmetric trans-aziridinations. Maruoka. *J. Am. Chem. Soc.* **2013**, *135*, 17667.



Palladium catalyzed asymmetric three-component coupling of boronic esters, indoles, and allylic acetates. Ready. *J. Am. Chem. Soc.* **2017**, *139*, 6038.



MIDA Boronates. (see M. Farmer, "Boron" GM 2014)

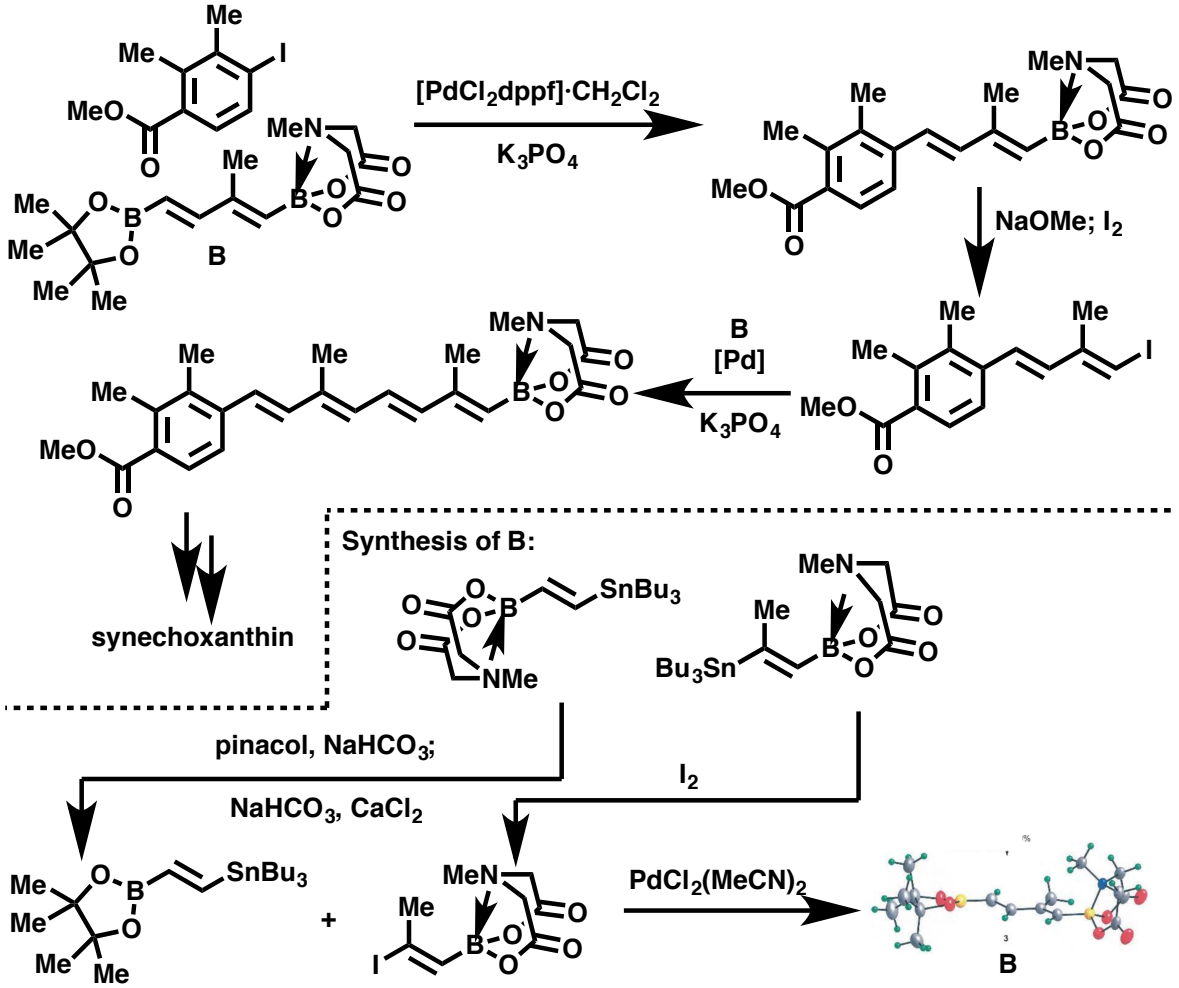
[initial report] A simple and modular strategy for small molecule synthesis: Iterative Suzuki–Miyaura coupling of B-protected haloboronic acid building blocks.
Burke. *J. Am. Chem. Soc.* **2007**, *129*, 6716.

- "indefinitely" bench-top stable under air
- chromotography compatible
- unreactive under standard anhydrous cross-coupling using either mild base
- rate of hydrolysis is (mostly) unaffected by substrate; can be controlled by reaction conditions

MIDA boronates are hydrolysed fast and slow by two different mechanisms.
Cheong, Burke, and Lloyd-Jones. *Nat. Chem.* **2016**, *8*, 1067.

Two distinct mechanisms.
1. Base-mediated: 3 orders of magnitude faster, RLS = attack by hydroxide at MIDA carbonyl C
2. Neutral: No exogenous acid or base, RLS = B–N cleavage by a small water cluster, $(H_2O)_n$

Total synthesis of synechoxanthin through iterative cross-coupling.
Burke. *Angew. Chem. Int. Ed.* **2011**, *50*, 7862.



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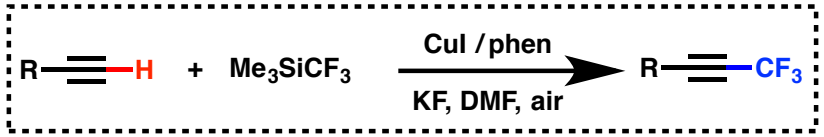
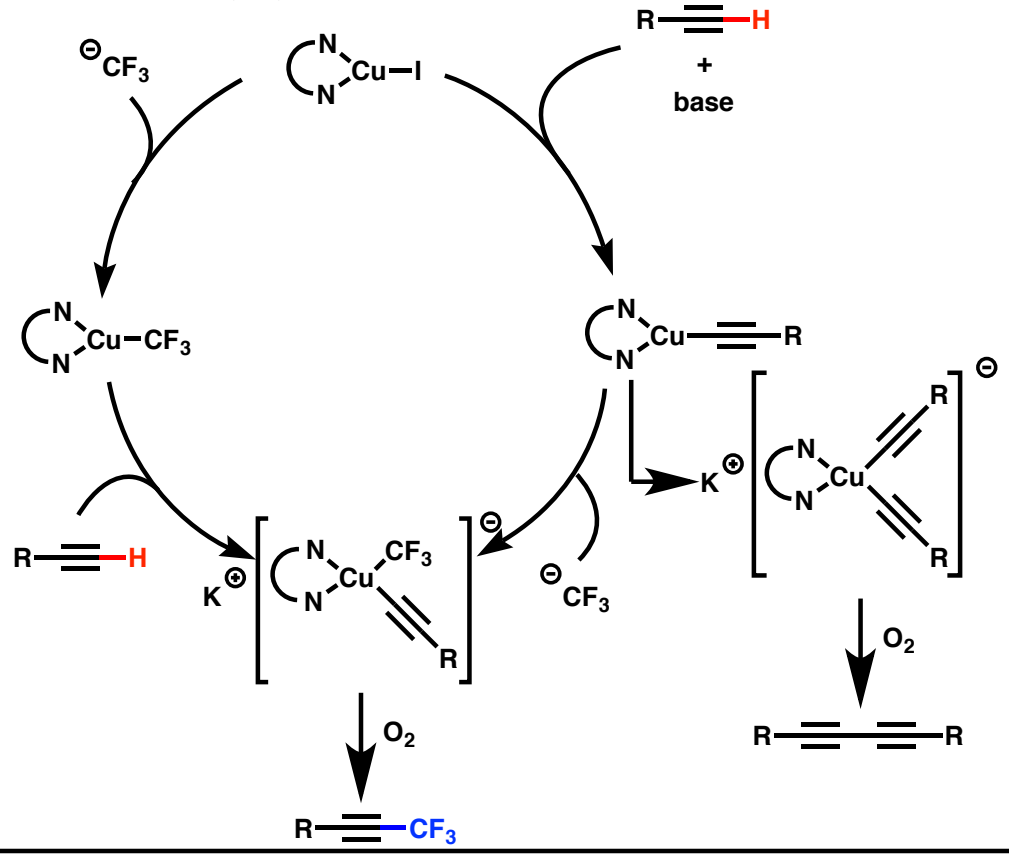
Cuprates.

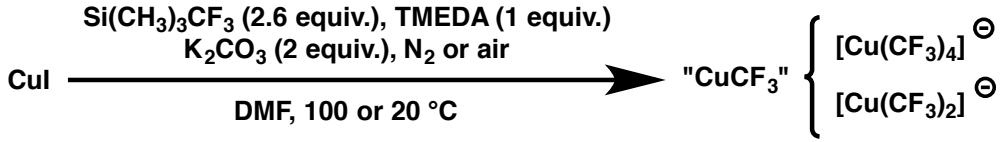
Copper-mediated aerobic oxidative trifluoromethylation of terminal alkynes with Me_3SiCF_3.
Qing. *J. Am. Chem. Soc.* **2010**, *132*, 7262.
The role of ate complexes in the copper-mediated trifluoromethylation of alkynes.
Koszinowski. *Chem. Eur. J.* **2016**, *22*, 11310.



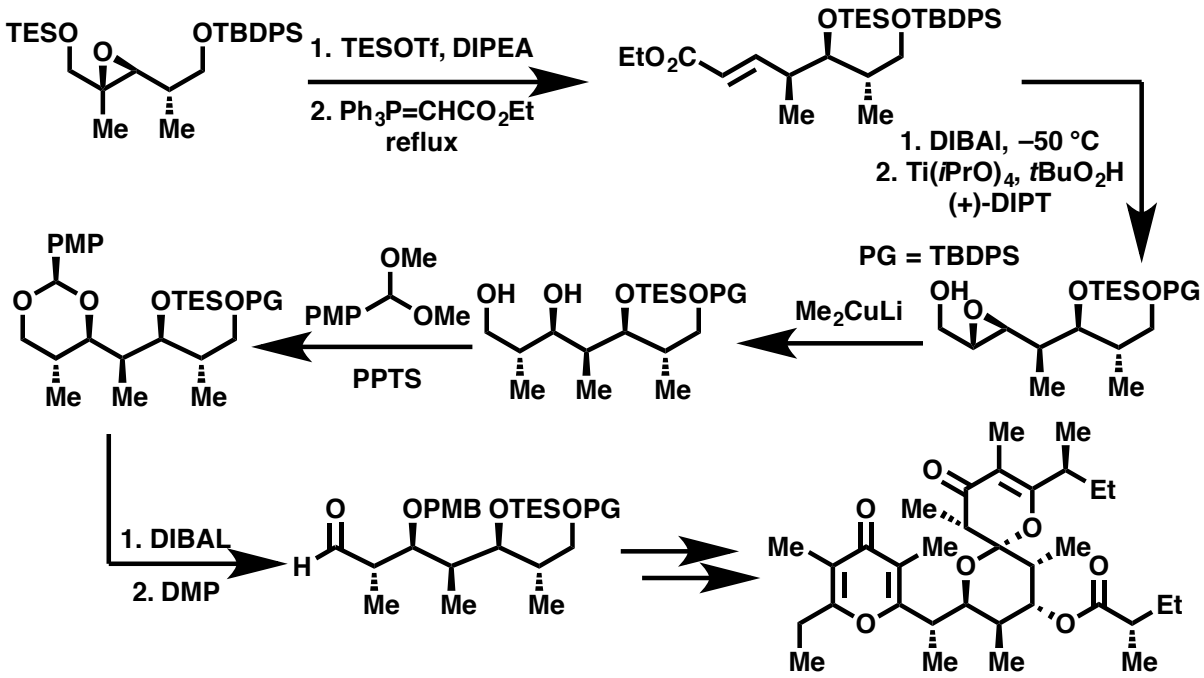
Oxidative trifluoromethylation and trifluoromethylthiolation reactions using (trifluoromethyl)trimethylsilane as a nucleophilic CF_3 source.
Qing. *Acc. Chem. Res.* **2014**, *47*, 1513.



Practical methods for the synthesis of trifluoromethylated alkynes: Oxidative trifluoromethylation of copper acetylides and alkynes.
Blanchard and Evano. *Adv. Synth. Cat.* **2014**, *356*, 2051.



Total synthesis of auripyrone B using a non-aldol aldol–cuprate opening process.
Jung. *Org. Lett.* **2010**, *12*, 2872.



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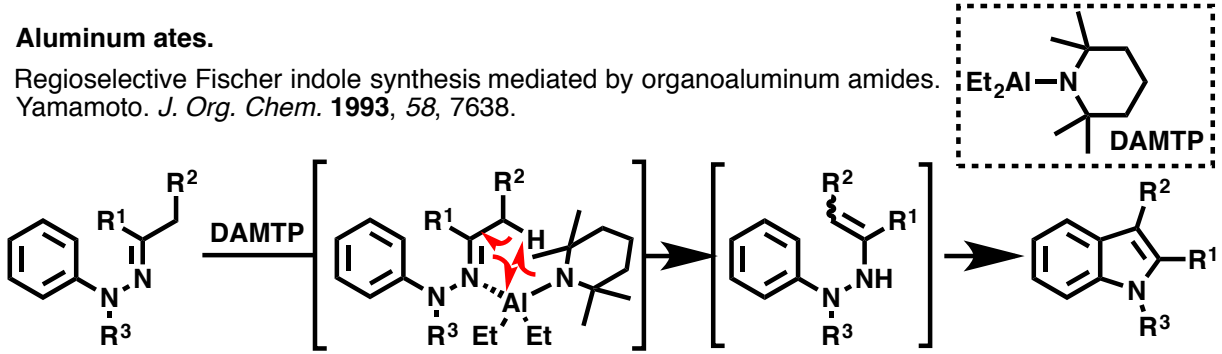
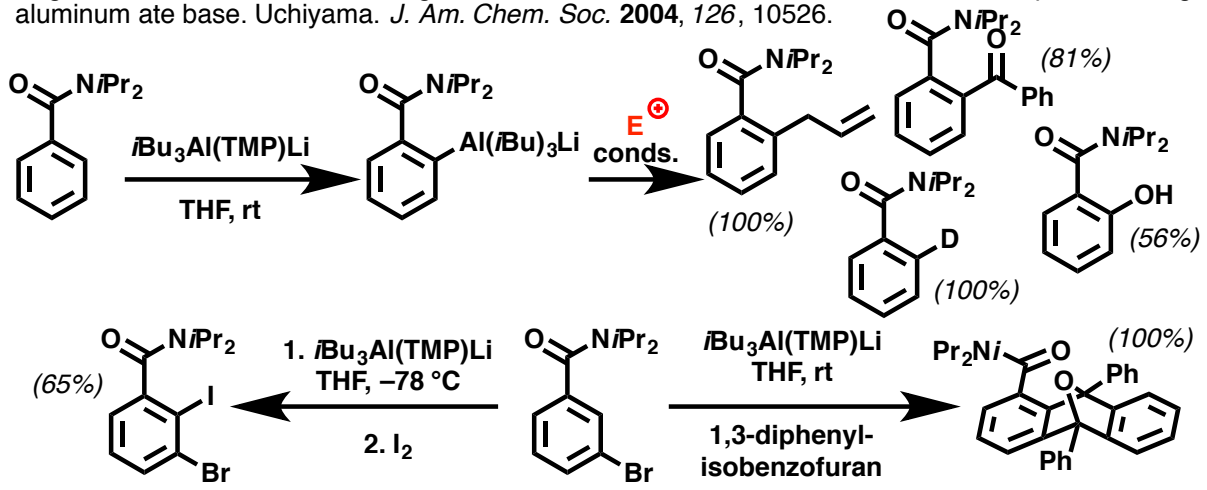
Aluminum ates.

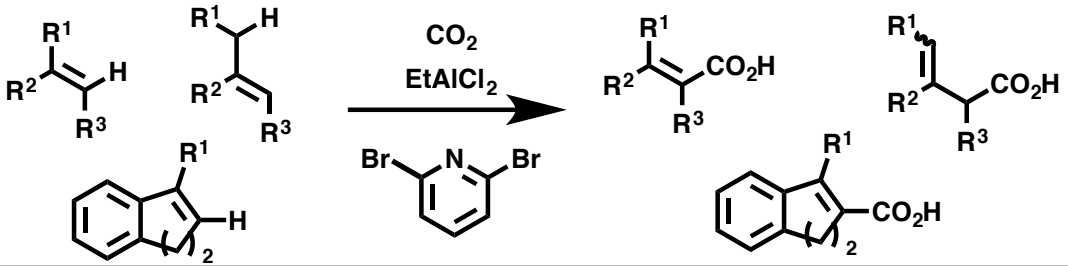
Regioselective Fischer indole synthesis mediated by organoaluminum amides.
Yamamoto. *J. Org. Chem.* **1993**, *58*, 7638.



Regio- and chemoselective direct generation of functionalized aromatic aluminum compounds using aluminum ate base. Uchiyama. *J. Am. Chem. Soc.* **2004**, *126*, 10526.

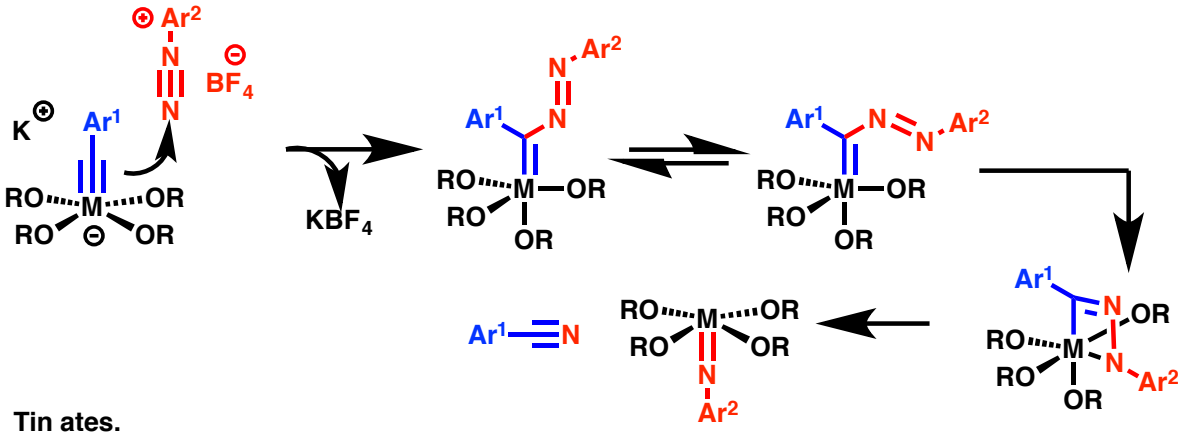


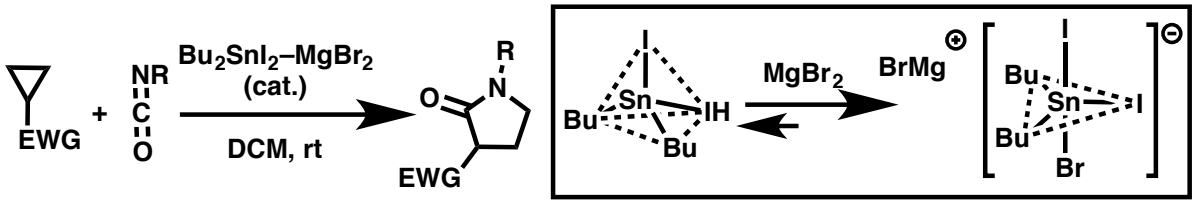
$EtAlCl_2$/2,6-disubstituted pyridine-mediated carboxylation of alkenes with carbon dioxide.
Tanaka, Hattori. *Org. Lett.* **2016**, *18*, 2576.



Molybdenum or tungsten alkylidyne ates.

The triple-bond metathesis of aryldiazonium salts: A prospect for dinitrogen cleavage.
Fürstner. *Angew. Chem. Int. Ed.* **2015**, *54*, 12814.



Tin ates.

Catalytic [3+2] cycloaddition through ring cleavage of simple cyclopropanes with isocyanates.
Shibata. *Org. Lett.* **2015**, *17*, 4010.